

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the reasons which follow.

Claims 23-26, 29 and 30 are pending in this application.

Double Patenting Rejection

The examiner has rejected claims 23-26 and 29-30 in light of US Patent 5,851,527 under the judicially created doctrine of obviousness type double-patenting. In response to this double patenting rejection, applicant is filing a terminal disclaimer with this response.

Rejection under 35 USC § 102(b)

The examiner has rejected claims 23-26 as being anticipated by Bagshawe KD *et al.* (WO 89/10140). As explained by the examiner, the Bagshawe reference teaches a three component system for the administration and treatment of cancer using an antibody directed enzyme prodrug therapy. The components in Bagshawe include a first component that attaches to malignant tumor cells, a second component that acts as a clearing agent for all unbound first components, and a third component that binds to the catalytic site of the first component. In contrast, the present application teaches a five component system for the treatment of cancer using an antibody directed enzyme prodrug therapy. These components are a first component which is a target protein that localizes at a target site, a second component that acts as a clearing agent for any unbound target protein, a third component that acts as an enzyme and forms a non-covalent targeting protein enzyme conjugate in situ, a fourth component that acts as a second clearing agent, and a fifth component that is a serum-soluble prodrug that the third enzyme component acts on to release a less soluble therapeutic agent at the target site.

As set forth above, unlike the prodrug therapy in Bagshawe which has an enzyme activating a substrate bound to the target tumor, the present application does not activate the targeting protein when it is bound by the enzyme. Rather, the

enzyme-substrate complex localizes and activates a later administered prodrug composition releasing a less soluble therapeutic agent.

Further, the prodrug composition administered in the present application is serum-soluble, but releases a lipophilic drug with low water solubility when it is activated by the enzyme released in step (c). Therefore, unlike the therapeutic agent in Bagshawe, the present application's therapeutic agent is less soluble than the administered prodrug decreasing the undesirable leakback from the target site to the bloodstream and keeping the therapeutic agent in the target locality. Because additional components are used in the present application than in the Bagshawe reference, because activation of the therapeutic agent occurs differently than the Bagshawe reference discloses, and because the therapeutic agent that is activated is less soluble than the administered prodrug, Bagshawe does not anticipate the present application.

Rejection under 35 USC § 103(a)

The examiner rejected claims 23-26 and 29-30 as being unpatentable over Bagshawe *et al.* in view of Tsuji *et al.* and Houba *et al.* As set forth above, the Bagshawe reference does not teach the use of a five component system, the activation of a prodrug composition by an enzyme/substrate compound, or the activation of a less soluble therapeutic agent from a soluble prodrug. Further, neither of the Tsuji or Houba references teaches any of these elements. Therefore, the present invention is not obvious to one of ordinary skill in the art because it utilizes components not suggested in the prior art, activates a separate compound than that which was suggested in the prior art, and results in a less soluble therapeutic agent localized in the target area than the prior art. There is no motivation whatsoever in any of the references for making such modification to Bagshawe.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.


The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

If any fees are due in connection with the filing of this Amendment, please charge the fees to our Deposit account No 19-0741. If a fee is required for an extension of time under CFR § 1.136 that is not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.